being gathered concerning safety and toxicity, the utilization of the agents at any given time seems to be a result of the forces of experience, emotion and fear of malpractice. The agents still remain an important mainstay of inhalation anesthesia.

Halothane continues to be widely used. Since its introduction in the late 1950's it has provided pleasant and safe anesthesia for millions of patients. The agent offers great flexibility, it is not unpleasant to smell, it is non-explosive, the incidence of nausea and vomiting is small, high concentrations of oxygen can be used. These are real and important advantages to physician and patient. In spite of considerable looking no one has found this drug to possess a higher mortality or morbidity rate than any other widely used approach to anesthesia for major operation.

The occurrence of "hepatitis" associated with use of halothane is apparently real. The most popular opinion is that this results from sensitization. Evidence for sensitization is its low incidence (one in thousands), lack of dose dependence, apparent increased incidence and rapidity of recurrence with repeated halothane use and failure to produce the lesion in laboratory animals. There is some recent evidence from chronic exposure at very low dosage, however, which suggests sensitization may not be the only factor responsible for hepatic injury.

Fluroxene has never been widely popular. In recent years evidence revealing higher values for blood pressure, cardiac output and alveolar ventilation has resulted in increasing use of this drug. There are now reports of hepatitis occurring with fluroxene, and the agent is explosive in the anesthetic range. Nausea and vomiting appear to be more common than with halothane. There are no data which relate the higher cardiorespiratory values to improved patient welfare, and this drug, which has been on the market for many years, does not appear to be headed for great popularity.

Methoxyflurane has been rather definitely associated with high output renal failure. Unlike the hepatic lesion of halothane, this lesion, available evidence in humans and laboratory animals suggests, is a reproducible, dose-dependent toxic protoplasmic effect. Low vapor pressure and high solubility are at once advantages and disadvantages of the agent. They do reduce its flexibility and versatility. As a result of this and the renal toxicity, methoxyflurane appears to be diminishing in clinical usage and importance.

Perhaps the most important aspect of the current status of these agents is the realization that they are metabolized to a large extent. Not many years ago, inhalation agents were thought to be excreted unchanged via the lungs. Now biodegradation is known to occur in surprisingly large fractions of the dosage administered. Metabolites or altered metabolic activity may explain much of the toxicity, idiosyncracy and species variability which has been characteristic of the evaluation of anesthetic agents over the years.

Suggestions have been made that contamination of operating room atmospheres may be responsible for abortions, hepatitis and perhaps other untoward events affecting operating room personnel. Without debating the validity of such claims, there is no firm evidence that halogenated agents are the important offenders.

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Dissociative Anesthesia

The need has been great for a method of producing analgesia and amnesia in patients for short periods of time without depressing respiration and circulation. To date ketamine is the best answer to this need since its use is characterized by catalepsy, amnesia and analgesia. The state has been designated as dissociative anesthesia since the patient truly seems disassociated from his environment. During this state blood pressure and pulse rate are more likely to be elevated than depressed. Minute volume of respiration usually is not decreased to a significant degree unless too large a dose is given too rapidly. Pharyngeal and laryngeal reflexes usually remain active enough to protect against aspiration of foreign material into the tracheo-bronchial tree.

Ketamine (Ketaject,® Ketalar®) is not the perfect agent and undoubtedly more satisfactory

drugs will become available for production of dissociative anesthesia. In some patients blood pressure elevation following administration of ketamine may be alarming. A few patients exhibit an excitement stage during induction and a greater number exhibit psychomotor activity during recovery that may require medication with phenothiazine, diazepam or barbiturate. The greatest deterent to the widespread use of ketamine has been the unpredictable unpleasant dreams that about 15 percent of patients experience during recovery. These can be diminished, but not predictably eliminated, by protection of the patient from undue sensory stimulation during recovery and the use of sedatives as discussed above.

At present the same precautions for monitoring and patient care must be available during dissociative anesthesia as during other conventional types of anesthesia.

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New Halogenated Anesthetics: Enflurane and Isoflurane

Two new halogenated ethers, enflurane (Ethrane,® CHFCl CF_2-O-CF_2H) and isoflurane (Forane,® CF_3 CHCl-O-CF_2H), are undergoing intensive studies with an eye toward introduction into clinical practice. They possess their own merits and offer reasonable alternatives to currently available inhalational anesthetics. The latter is important because of concern about flammability or toxic effects of various accepted agents. Enflurane has received fairly broad clinical use whereas isoflurane is undergoing intensive clinical trials.

Since their chemical structures are so alike one might expect similar properties. They possess similar, relatively low solubility in blood and lipids, are nonflammable and are highly stable in the bottle and in the presence of alkali. Both preserve myocardial function and cause vasodilatation. The latter predominates so that arterial pressure is generally less than awake values in the unstimulated subject. Respiratory depression occurs with both to a degree as great as or greater than available agents. Both depress neuromuscular function. Isoflurane is more depressant to neuromuscular function by itself or in combination with neuromuscular blocking agents than halothane. Relatively small doses of muscle relaxant drugs are needed to provide adequate surgical conditions.

Despite similar physical characteristics enflurane and isoflurane differ significantly in their effects. Isoflurane is less susceptible to biodegradation than enflurane. Isoflurane's lack of metabolism makes it unique among halogenated anesthetics and may make its highly halogenated nature less worrisome. Enflurane sensitizes the myocardium to the arrhythmic effects of epinephrine but isoflurane does not. Both agents induce prominent EEG burst suppression. However, enflurane anesthesia is characterized by increasing EEG wave frequency as anesthetic dose increases, by high voltage spikes and, occasionally, by seizure patterns. Muscle twitches and muscle seizure activity have occurred. The muscle activity usually signifies presence of relatively deep anesthesia or hypocarbia or both and can be stopped by reversal of the latter events. The central nervous system effects are not associated with cerebral ischemia or injury. This innocuousness lends credence to the view that enflurane's EEG effects, although somewhat unique, are in the spectrum of normal anesthetic effects.

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Patient Monitoring

The standard vital signs of blood pressure, pulse, respiration and temperature have been valuable in assessing patients' conditions and problems for many decades. With modern electronics, the electrocardiogram has been a useful addition to the constant monitoring of patients, especially in detecting arrhythmias early and establishing therapy or preventive maintenance. The electroencephalogram has been a disappointment because of the difficulties with artifacts